

In the Specification

Please insert the following heading and paragraph after the title of the application on page 1 of the specification:

--Cross Reference to Related Applications

This application is a continuation of U.S. Serial No. 09/508,923, filed June 19, 2000, which claims priority from International Application No. PCT/GB98/02834, filed September 18, 1998. These applications, in their entirety, are incorporated herein by reference.--

At page 4, please amend the paragraph starting at line 22 as follows:

Fig. 1 shows the effect of pH and ageing on percentage phosphate binding of mixed metal compounds. In Fig. 1,

○	Mg:Fe	3:1	prep 2 unaged
●	Mg:Fe	3:1	prep 2 aged
△	Mg:Fe	2:1	prep 1 unaged
▲	Mg:Fe	2:1	prep 1 aged
□ ☒	Ca:Fe	3:1	unaged
■	Ca:Fe	3:1	aged
★	Ca:Fe:Mg		unaged
★	Ca:Fe:Mg		aged

At page 5, please amend the paragraph beginning at line 12 as follows:

Fig. 3 shows the effect of increasing weight of compound on percentage phosphate bound at pH3. In Fig. 3,

▲-▲ Mg(OH)₂
Δ- Δ Mg:Fe 2:1 Prep unaged wet
○-○ CT100

- CaFe 3:1 Aged wet
- ALTACITE Altacite liquid washed
- *-* Al(OH)₃

At page 5, please amend the paragraph beginning at line 20 as follows:

Fig. 4 shows the effect of increasing weight of compound on percentage phosphate bound at pH7. In Fig. 4,

- CaFe 3:1 Aged wet
- CT100
- ALTACITE Altacite liquid washed
- *-* Al(OH)₃

At page 5, please amend the paragraph beginning at line 26 as follows:

Fig. 5 shows the time course of phosphate binding in food. In Fig. 5,

- Al(OH)₃
- CT Fe:Mg 2:1 unaged washed
- ▲ Ce(OH)₃
- ▼ ALTACITE Altacite liquid unwashed
- ◊ Mg(OH)₂
- ★ Milk of Magnesia (1.8g Mg(OH)₃)
- ★ CT100 washed

At page 9, please amend the paragraph beginning at line 15 as follows:

Compounds tested:

- (1) a hydroxy carbonate containing a 2:1 ratio Mg: Fe
- (2) a hydroxy carbonate containing a 3:1 ratio of Mg: Fe
- (3) a hydroxy carbonate containing a 3:1 ratio of Ca: Fe
- (4) a hydroxy carbonate containing a 3:3:2 ratio of Ca: Mg: Fe
- (5) CT100, a hydrotalcite of the formula Al₂Mg₆(OH)₁₆CO₃.4H₂O
- (6) ALTACITE Altacite, a hydrotalcite of the same formula as CT 100,

commercially available from Roussell, in the form of an aqueous slurry

- (7) magnesium hydroxide
- (8) aluminum hydroxide.

At page 1, please amend the paragraph beginning at line 11 as follows:

In patients with kidney failure on haemodialysis (of whom there are 6,000,000 world wide), phosphate concentrations in the blood plasma can rise dramatically and such hyperphosphataemia can result in calcium phosphate deposition in soft tissue. Currently, the plasma phosphate levels are reduced by oral intake of inorganic and organic phosphate binders. The most common treatment in the UK is with aluminium aluminum hydroxide gel (“AludroxALUDROX®” at 4 g/day) which forms an insoluble aluminium aluminum phosphate. However, this results in further toxic complications due to Al accumulation, eg reduction in haemoglobin production, impairment in natural repair and production of bone and possible impairment of neurological/cognitive function. Improvements in phosphate binding capacity as compared with aluminium aluminum hydroxide gel have been achieved with other aluminium aluminum compounds such as microcrystalline aluminium aluminum oxide hydroxide (boehmite) and certain hydrotalcites have been made; Ookubo et al, Journal Pharmaceutical Sciences (November 1992), 81(11), 1139-1140. However, such compounds still result in an intolerable amount of aluminium aluminum accumulation in renal failure patients. It is also known to use calcium compounds having pool solubility at pH 6-9, eg calcium carbonate, hydroxide, oxide and/or sulphate in a medicinal form

At page 5, please amend line 18 as follows:

- Altacite ALTACITE liquid washed

At page 5, please amend line 24 as follows:

- Altacite ALTACITE liquid washed

At page 6, please amend line 1 as follows:

▼ Altacite ALTACITE liquid unwashed

At page 9, please amend the paragraph beginning at line 22 as follows:

(6) Altacite ALTACITE, a hydrotalcite of the same formula as CT 100, commercially available from Roussell, in the form of an aqueous slurry

At page 10, please amend the paragraph beginning at line 13 as follows:

Method 3 – Milk (250 ml), cornflakes (50 g), bread (2 slices) and ~~marmite~~ MARMITE (yeast extract) (5 g) were mixed in a stomacher for 30 minutes containing 0.01 M HCl (so as to simulate the conditions in the stomach). A 20 ml aliquot of food was removed and centrifuged. Phosphate was measured in the supernatant. Two grams of the phosphate binder compound was added to the bulk food slurry and mixed for a further 30 minutes. An aliquot of food was taken and the phosphate measured in the supernatant following centrifugation. Further aliquots were taken after a further 30 and 90 minutes mixing.

At page 10, please amend the paragraph beginning at line 21 as follows:

In each of the above methods, for each of the compounds (1)-(4), where a dry powder was dosed as the phosphate binder, phosphate binding was measured for a given dosage measured after drying to constant weight at 40°C. Where a wet cake was dosed (or Altacite ALTALCITE (6) added), an amount equivalent to a given constant dry weight at 40°C was used. For known commercially available binders, a given weight of the material supplied

At page 13, please amend the paragraph beginning at line 4 as follows:

The compounds Mg:Fe 2:1 (1), Ca:Fe 3:1 (2) and CT100 (5) all bound up to 60-70% of the phosphate. Interestingly, the CT100 bound – 50% more phosphate at any weight than the Altacite ALTACITE (6), despite an identical molecular formulae.

At page 13, please amend the paragraph beginning at line 15 as follows:

At pH 7, the Mg:Fe 3:1 compound (2) was the best phosphate binder over the range of weights studied. The CT100 (5) bound at least twice as much phosphate than the Altacite ALTACITE (6) at any weight studied.

At page 16, please amend the paragraph beginning at line 7 as follows:

The metals in the solutions/suspensions described in Table 4 2 were precipitated at the same time by the addition of sodium hydroxide. A preparation was also made by precipitating the calcium and iron separately with sodium hydroxide, the precipitates were then mixed. For this, $\text{Fe}_2(\text{SO}_4)_3$ (1 mole) and NaOH (6 moles) were mixed in 4 litres deionised H_2O . In a separate 4 litres of water, CaSO_4 (6 moles), NaOH (12 moles) and Na_2CO_3 (5 moles) were mixed. These two suspensions were then fed into the flask with an overflow at -2 litres and constantly mixed.

At page 39, please amend the paragraph beginning at line 3 as follows:

Urine and serum aluminium aluminum concentrations were measured using graphite furnace furnace atomic absorption spectroscopy. For the animals taking $\text{Al}(\text{OH})_3$ or CT100, mean serum aluminum concentrations were not significantly higher than serum aluminium aluminum from control animals (Table 12). Surprisingly, animals treated with CTFeca and CTFeMg showed the highest mean serum aluminium aluminum concentrations, both significantly higher than animals treated with $\text{Mg}(\text{OH})_2$, $\text{Al}(\text{OH})_3$, CaCO_3 or controls.